

# PATENT COOPERATION TREATY

SBD

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
KOWALCHYK, KATHERINE, M.  
MERCHANT & GOULD P.C.  
P.O. BOX 2903  
MINNEAPOLIS, MN 55402-8844

## PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

ATK RESP SR/WO: November 2, 2008 DV

Applicant's or agent's file reference  
103201-10601 40390.0009WOU1

Date of mailing  
(day/month/year)

**FOR FURTHER ACTION** See paragraphs 1 and 4 below

International application No.  
PCT/US07/79051

International filing date  
(day/month/year) 20 September 2007 (20.09.2007)

Applicant  
DHARMACON, INC.

**DEMAND DUE: December 2, 2008** SDP

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 338.82.70.

**For more detailed instructions,** see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/US  
Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
Facsimile No. (571) 273-3201

Authorized officer

JENNIFER PITRAK

Telephone No. 5712703061

Form PCT/ISA/220 (January 2004)

(See notes on accompanying sheet)

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
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SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing  
(day/month/year)

02 SEP 2008

Applicant's or agent's file reference  
103201-10601

**FOR FURTHER ACTION** See paragraphs 1 and 4 below

International application No.  
PCT/US07/79051

International filing date  
(day/month/year) 20 September 2007 (20.09.2007)

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In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

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P.O. Box 1450  
Alexandria, Virginia 22313-1450  
Facsimile No. (571) 273-3201

Authorized officer

JENNIFER PITRAK

Telephone No. 5712703061

Form PCT/ISA/220 (January 2004)

(See notes on accompanying sheet)

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|   |  |   |
|---|--|---|
| Applicant's or agent's file reference<br>103201-10601 | <b>FOR FURTHER ACTION</b><br><small>see Form PCT/ISA/220<br/>as well as, where applicable, item 5 below.</small> |   |
| International application No.<br>PCT/US07/79051       | International filing date ( <i>day/month/year</i> )<br>20 September 2007 (20.09.2007)                            | (Earliest) Priority Date ( <i>day/month/year</i> )<br>29 November 2006 (29.11.2006) |
| Applicant<br>DHARMA CON, INC.                         |  |   |

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 2 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the Report**

a. With regard to the **language**, the international search was carried out on the basis of:

☒

the international application in the language in which it was filed.

☐

a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 Rule 43.6 *bis(a)*

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☐ **Unity of invention is lacking** (See Box No. III)

4. With regard to the **title**,

☒

the text is approved as submitted by the applicant.

☐

the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒

the text is approved as submitted by the applicant.

☐

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

☐

as suggested by the applicant.

☐

as selected by this Authority, because the applicant failed to suggest a figure.

☐

as selected by this Authority, because this figure better characterizes the invention.

☒

none of the figures is to be published with the abstract.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/79051

A. CLASSIFICATION OF SUBJECT MATTER  
IPC: C07H 21/02( 2006.01)

USPC: 536/23.1  
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 536/23.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
CAPLUS, MEDLINE, BIOSIS, EMBASE, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| X          | US 2005/0176024 A1 (McSwiggen, et al.) 11 August 2005 (11.08.2005), p.4 paragraph 21; p.6, paragraph 34; p.18, paragraph 118; p.26, paragraph 187; p.41, paragraph 315. | 1-27                  |
| X          | US 2006/0094032 A1 (DeFougerolles, et al.) 04 May 2006 (04.05.2006), pages 2-3 and page 12, paragraphs 176-183.   | 1-27                  |

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

| * Special categories of cited documents:  |  |
|---|--|
| "A" document defining the general state of the art which is not considered to be of particular relevance  | "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| "E" earlier application or patent published on or after the international filing date   | "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "O" document referring to an oral disclosure, use, exhibition or other means  | "&" document member of the same patent family  |
| "P" document published prior to the international filing date but later than the priority date claimed  |  |

Date of the actual completion of the international search  
11 August 2008 (11.08.2008)

Date of mailing of the international search report

02 SEP 2008

Name and mailing address of the ISA/US  
Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
Facsimile No. (571) 273-3201

Authorized officer

JENNIFER PITKIN

Telephone No. 571 2703061

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

# PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:  
KOWALCHYK, KATHERINE, M.  
MERCHANT & GOULD P.C.  
P.O. BOX 2903  
MINNEAPOLIS, MN 55402-8844

Date of mailing  
(day/month/year) **02 SEP 2008**

Applicant's or agent's file reference

103201-10601

**FOR FURTHER ACTION**

See paragraph 2 below

International application No.

PCT/US07/79051

International filing date (day/month/year)

20 September 2007 (20.09.2007)

Priority date (day/month/year)

29 November 2006 (29.11.2006)

International Patent Classification (IPC) or both national classification and IPC

IPC: **C07H 21/02** (2006.01)

USPC: 536/23.1

Applicant

DHARMACON, INC.

1. This opinion contains indications relating to the following items:

- |                                     |              |  |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion   |
| <input type="checkbox"/>            | Box No. II   | Priority   |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability   |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention   |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited  |
| <input checked="" type="checkbox"/> | Box No. VII  | Certain defects in the international application   |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application  |

## 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Date of completion of this opinion

11 August 2008 (11.08.2008)

Authorized officer

JENNIFER PETERSON

Telephone No. 5712703061

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US07/79051

**Box No. I Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ on paper

☐ in electronic form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in electronic form.

☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US07/79051

**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

|                               |                    |     |
|-------------------------------|--------------------|-----|
| Novelty (N)                   | Claims <u>NONE</u> | YES |
|                               | Claims <u>1-27</u> | NO  |
| Inventive step (IS)           | Claims <u>NONE</u> | YES |
|                               | Claims <u>1-27</u> | NO  |
| Industrial applicability (IA) | Claims <u>1-27</u> | YES |
|                               | Claims <u>NONE</u> | NO  |

2. Citations and explanations:

Claims 1-27 lack novelty under PCT Article 33(2) as being anticipated by McSwiggen, et al.

Claims 1-27 lack novelty under PCT Article 33(2) as being anticipated by De Fougères, et al.

The claims are to siRNA-cholesterol conjugates and methods of using the conjugates. The siRNAs comprise mismatches, 2'-O-methyl- and 2'-F-modified nucleotides, phosphate moieties, and overhangs. The conjugates comprise the siRNA linked via a 5-8-atom linker molecule to cholesterol, wherein the linkage is at the 3' end of the sense strand and wherein the siRNA further comprises a dye molecule attached to the 5' end of the sense strand.

Both McSwiggen, et al. and De Fougères, et al. independently teach siRNAs comprising mismatches, 2'-O-methyl- and 2'-F-modified nucleotides, phosphate moieties, and overhangs. Both McSwiggen, et al. and De Fougères, et al. teach conjugates comprising siRNA linked to cholesterol and dyes, wherein the linkage is at either the 3'- or the 5'-end of the sense strand. Both references teach that the siRNA conjugates exhibit improved cellular delivery over non-conjugated siRNAs.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US07/79051

**Box No. VII Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

Claim 10 is objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: the term "cojunate" appears to be a misspelling.